



INTRAVENOUS ENDOTHELIAL-LIKE CELLS DIFFERENTIATED FROM MESENCHYMAL STEM CELLS ACCELERATE RE-ENDOTHELIZATION IN BALLOON-INJURED RAT

ACC Poster Contributions
Georgia World Congress Center, Hall B5
Tuesday, March 16, 2010, 9:30 a.m.-10:30 a.m.

Session Title: Angiogenesis
Abstract Category: Vascular--Pathophysiology--Basic/Angiogenesis/Gene Therapy
Presentation Number: 1275-358

Authors: *Ki-Chul Hwang, Min-Ji Cha, Heesang Song, Byeong-Wook Song, Eunju Choi, Onji Ham, Namsik Chung, Yangsoo Jang, Ki-Chul Hwang, Cardiovascular Research Institute, Division of Cardiology, Yonsei University College of Medicine, Seoul, South Korea*

Background: Recent studies suggested the potential of EPCs for neovascularization and re-endothelization, but the difficulty of obtaining sufficient cells has been an obstacle to the therapeutic use of blood-derived EPCs. MSCs have great advantages for cell therapy such as ease of preparation and great plasticity. In this study, we hypothesize that small molecules induce MSCs differentiation into endothelial like cells through regulating protein kinase activity and the differentiated cells show the greater beneficial effects on the re-endothelization in balloon-injured rat model.

Methods & Results: We screened chemical libraries and found that subfamily of GSK3 β inhibitors cause recognizable changes in the differentiation rates of MSCs to endothelial cells. Among them, SB-216763 showed the greatest effect on endothelial differentiation. SB-216763 greatly increased the expression of endothelial markers such as CD34, eNOS, VE-cadherin, VCAM-1, and VEGF-R2 in MSCs. Moreover, we observed that SB-216763 treated MSCs showed the greater formation of capillary-like structures compared to un-treated MSCs. SB-216763 led to depletion of S-phase cells and decreased overall proliferation of MSCs. We next examined if the differentiated cells increase the beneficial effects on vascular repair in the balloon-injured rats. MSCs or differentiated endothelial like cells were injected intravenously and the extent of vascular re-endothelization was then assessed at 2 weeks after the injection. The denuded area was markedly reduced in the injured vessels of rat injecting endothelial like cells compared with control mice receiving MSCs. Immunohistochemical analysis of the endothelial marker CD31 also demonstrated accelerated re-endothelization of the injured artery in the endothelial like cells-injected group when compared with that in the MSCs group.

Conclusions: The inhibition of GSK-3 β activity leads to the differentiation of MSCs into endothelial cells and the injection of differentiated cells accelerates the re-endothelization in the balloon-injured rat. This system offers a novel understanding of MSC biology and the potential for the development of new regenerative medicines.